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EXAMINER				
LEA, CHRISTOPHER RAYMOND				
ART UNIT		PAPER NUMBER		
1619				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IPDocket@gibbonslaw.com

Office Action Summary

Application No.

10/577,197

Applicant(s)

GRUBER ET AL.

Examiner

Christopher R. Lea

Art Unit

1619

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 January 2009 and 12 March 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 3-6 and 8-41 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3-6 and 8-41 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 April 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

This application is a 371 (national stage application) of PCT/CH04/00655.

Receipt of Amendments/Remarks filed on January 16 and March 12, 2009, is acknowledged. In response to Non-final office action dated December 23, 2008, applicant amended claims 1, 3, 8, 9, 11-13, 16, 17, 20, 24, 25, 27, 31, & 41, canceled claims 2 & 7, and added no new claims. Claims 1, 3-6, & 8-41 are pending. Claims 1, 3-6, & 8-41 are under examination.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. All new rejections applied have been necessitated by applicant's amendment to the claims. They constitute the complete set presently being applied to the instant application.

Priority

1. The examiner acknowledges the receipt of the application data sheet and amendment to the specification filed January 16, 2009, and subsequent amendment to the specification (to correct a typographical error) filed March 12, 2009. These filings are sufficient to overcome the objections raised by the examiner in the Office Action dated December 24, 2008.
2. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 2, 3-6, 8-29 & 33-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuramoto et al. (US Patent 5,470,580) in view of Panoz et al. (US Patent 5,051,262).

Applicant claims

Applicant claims a non-effervescent tablet that comprises sodium naproxen and a basic auxiliary agent. Applicant further claims excipients added to the tablet as well as percentages for several of the components.

Determination of the scope and content of the prior art (MPEP 2141.01)

Kuramoto et al. teach, as a whole, tablets containing naproxen sodium.

Claims 1, 3, 4, 8-13: Kuramoto et al. teach a tablet containing sodium naproxen in an of 80-90% and 2-20% auxiliary components (column 7, lines 32-44). Kuramoto et al. also teach that the tablet may optionally be film-coated (column 8, line 35).

Claims 5 & 6: Kuramoto et al. teach a water content of 6-8% (column 7, lines 32-44).

Claims 14-25: Kuramoto et al. teach povidone (non-crosslinked polyvinylpyrrolidone) and starch as binders (fillers) in the tablet (column 5, lines 11-34). Kuramoto et al. teach using 1-6% binder (filler) in the tablet (column 7, lines 32-44). The proportions claimed outside this range are not so disparate that the skilled artisan would expect different properties to be imparted to the composition as a whole.

Claims 26 & 27: Kuramoto et al. teach using croscarmellose as a disintegrant in the tablet (column 5, lines 43-45).

Claim 28: Kuramoto et al. teach including a lubricant and/or glidant in the tablet composition (column 5, lines 55-57).

Claim 29: Kuramoto et al. teach that lubricants/glidants are not essential to the invention, thereby teaching possible embodiments that contain not lubricant or glidant (column 7, lines 45-56).

Claim 33: Kuramoto et al. teach a tablet with granule size of 100-350 microns (.1 to .35 mm) (example 1, column 9, line 10).

Claim 34: Kuramoto et al. teach a tablet with hardness of at least 5 S.C. units (35 N) (example 1, column 9, line 11-12).

Claim 35: The claimed amount of the active agent component is a result-effective parameter chosen to obtain the desired effects and controllable through the size of the tablet made, all of which are within the purview of the skilled artisan to determine.

Claim 36: Kuramoto et al. teach that the tablet may consist essentially of 100% naproxen sodium (column 7, lines 45-56).

Claims 37-40: Kuramoto et al. teach naproxen sodium tablets comprising *inter alia* microcrystalline cellulose, croscarmellose (both column 5, lines 43-45), talc, and magnesium stearate (column 5, lines 55-57). Kuramoto et al. teach water-soluble cellulose derivatives, such as a hydroxypropyl cellulose, as suitable binders (column 5, lines 11-15). The claimed amounts and proportions of the auxiliary agent components are result-effective parameters chosen to obtain the desired effects and optimizable through routine experimentation.

Claim 41: Kuramoto et al. teach a method of making a tablet where naproxen sodium (80-90%) is combined with auxiliary agent components and compressed into a tablet (claim 7).

**Ascertainment of the difference between the prior art and the claims
(MPEP 2141.02)**

The difference between the teachings of Kuramoto et al. and the instant claims is that Kuramoto et al. do not teach adding a basic auxiliary agent to the tablet. This deficiency in Kuramoto et al. is cured by the teachings of Panoz et al.

Panoz et al. teach, as a whole, adding pH adjustors to active agents to improve the release of the agents.

Claims 1, 2, 3-6, 8-29 & 33-41: Panoz et al. teach adding pH-adjusting compounds to dosage forms, thereby creating a microenvironment around the medicament, causing the medicament to have optimum solubility independent of the pH of the surrounding region of the gastro-intestinal tract (column 2, lines 56-65). Panoz et al. teach naproxen among the drugs that would benefit from the addition of a basic pH adjustor (column 5, lines 41-56). Panoz et al. teach alkaline bicarbonates (which include sodium hydrogen carbonate) among the basic pH adjustors (column 5, lines 57-65). The claimed amounts and proportions of the basic auxiliary agent are result-effective parameters chosen to obtain the desired effects.

**Finding of *prima facie* obviousness
Rationale and Motivation (MPEP 2142-2143)**

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to add a basic auxiliary agent (such as sodium hydrogen carbonate) as taught by Panoz et al. to the naproxen tablets taught by

Kuramoto et al. to improve the solubility of the naproxen and produce the instant invention. The skilled artisan would have been motivated to do this because Panoz et al. teach naproxen among the drugs that would benefit from the addition of a basic pH adjustor.

From the teachings of the references and in the absence of evidence to the contrary, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in adding sodium hydrogen carbonate to the naproxen sodium tablet and producing the claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

7. Claims 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuramoto et al. and Panoz et al. as applied to claim 1 above, and further in view of Patel et al. (US PreGrant Publication 2003/0180352).

Applicant claims

Applicant claims a tablet containing naproxen sodium and a basic auxiliary agent further comprising a tenside (surfactant).

**Determination of the scope and content of the prior art
(MPEP 2141.01)**

Since claims 30-32 depend from claim 1, rejection of claim 1 under 35 USC 103 is also appropriate. Detailed discussion of the rejection of claim 1 and the teachings of Kuramoto et al. and Panoz et al. appears above.

**Ascertainment of the difference between the prior art and the claims
(MPEP 2141.02)**

The difference between the combined teachings of Kuramoto et al. and Panoz et al. and the instant claims is that Kuramoto et al. and Panoz et al. do not teach adding a surfactant to the tablet. This deficiency in Kuramoto et al. and Panoz et al. is cured by the teachings of Patel et al.

Patel et al. teach, as a whole, solid carriers for improved delivery of active agents in pharmaceutical compositions.

Patel et al. teach adding ionic and/or non-ionic surfactants to solid dosage forms as means to improve the stability and dissolution profile of the active agent (paragraph 144). Among the preferred ionic surfactants taught by Patel et al. is sodium lauryl (dodecyl) sulfate (paragraph 191). The claimed amounts and proportions of the tenside (surfactants) are result-effective parameters chosen to obtain the desired effects.

**Finding of *prima facie* obviousness
Rationale and Motivation (MPEP 2142-2143)**

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to add a surfactant as taught by Patel et al. to the tablet taught by the combination of Kuramoto et al. and Panoz et al. to improve the

solubility and bioavailability of the active agent and produce the instant invention. The skilled artisan would have been motivated to add a surfactant because Patel et al. teach that adding a surfactant to solid dosage form can provide increased solubility of the active ingredient in the solid carrier; improved dissolution of the active ingredient; improved solubilization of the active ingredient upon dissolution; enhanced absorption and/or bioavailability of the active ingredient, particularly a hydrophilic active ingredient; and improved stability, both physical and chemical, of the active ingredient..

From the teachings of the references and in the absence of teachings to the contrary, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in adding a surfactant to the tablet containing naproxen sodium and a basic auxiliary agent and producing the claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

Applicant's arguments filed March 12, 2009, have been fully considered but they are not persuasive. Applicant argues that 1) Panoz et al. teach away from the addition of an alkaline pH-adjusting agent to naproxen sodium and 1) Patel et al. teach away from the invention by implying lower amounts of basic auxiliary agent to be used.

As to 1), the examiner believes that applicant has mischaracterized the teachings of Panoz et al. Panoz et al. teach that the choice of basic or acidic pH adjustor is

dependent on the characteristics of the drug, not the active agent as a whole. The examiner's position is buoyed by example 1, where Panoz et al. state:

Quinidine sulphate is a salt of a basic drug. As such it is more soluble in an acidic environment than in a basic environment. Without a pH-adjusting agent the solubility of this drug in alkaline solutions, and hence in the small intestine (where most absorption takes place), is low. The addition of an acidic pH-adjusting agent therefore increases the area of the gastro-intestinal tract over which the drug is absorbed and thus improves the blood level profile. (column 6, lines 60-68)

The skilled artisan would not consider a sulfate ion to be responsible for the activity of quinidine sulfate. Indeed throughout all the examples taught by Panoz et al., it is the nature of the active component that determines the pH adjustor. Likewise, these teachings of Panoz et al. would motivate the skilled artisan to add a basic pH adjustor to a naproxen-containing composition regardless of whether the naproxen in said composition was the free acid or sodium salt.

As to applicant's argument that Panoz et al. teach a slowing down of dissolution upon the addition of a basic pH adjustor, this is irrelevant. The method of Panoz et al. is designed to cause pH independent release of the drug (note in figure 17, how lines d, e, & f are similar despite pH differences) to ensure dissolution regardless of location in the gastrointestinal tract. This is clearly a desirable property, though it differs from applicant's stated goal of speedy dissolution. Therefore, the skilled artisan would again have had motivation to add a basic pH adjustor.

As to 2), the examiner does not agree with applicant's characterization of the teachings of Patel et al. with respect to eliminating the stabilizer. Though Patel et al. teach that the amount of stabilizer required for efficacy may be reduced by the addition

of a surfactant, it does not appear to teach elimination (perhaps this is taught in the location referred to by "19/20" on page 13 of the remarks, the examiner does not understand what is meant by that notation) rather that the number of substances which might serve as stabilizers is increased.

For all the above reasons the rejections under 35 U.S.C. 103(a) are maintained.

Conclusion

Claims 1, 3-6, & 8-41 are rejected. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher R. Lea whose telephone number is (571) 270-5870. The examiner can normally be reached on Mon-Thu 7:30-5:00 ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571)272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CRL
/Johann R. Richter/
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